the full-length pseudogene genomic DNA were used as control templates (Choudary et al. 1986). The forward primer sequence from exon 2 was 5′-AGGCAGTGTC-GTGGGCATCA-3′ (1F), and the reverse primer sequence from exon 11 was 5′-GAGGCACATCCTTA-GAGGAG-3′ (2R), each of which contain sequence complementary and common to both the gene and pseudogene. The PCR product was electrophoretically separated on a 0.7% agarose gel, individual bands were excised, and DNA was extracted using a Geneclean II Kit (Bio 101) for direct sequencing and mutation analyses.

This amplification technique should aid the clinician by simplifying the molecular analysis of the glucocerebrosidase gene and contribute to a better understanding of the clinical heterogeneity encountered in Gaucher disease (Sidransky and Ginns 1993). In some instances, alleles with deletions, fusions, or duplications may be detected by this method and will result in additional smaller or larger bands. Previously, investigators were limited by the need to custom design primers from regions where the gene and pseudogene differed by mismatches or deletions. Using long PCR to clearly separate the two sequences, we can more reliably evaluate sequence exclusively from the functional gene and have successfully identified several rare and novel mutations. Long-template PCR may similarly prove useful in the study of other genes with nearby highly homologous pseudogene sequences.

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The Genetics of Traditional Living: Y-Chromosomal and Mitochondrial Lineages in the Sinai Peninsula

To the Editor:

Two parts of the human genome are unique in that they lack recombination and are inherited through only one sex: (1) the Y chromosome, which is paternally inherited and lacks recombination except in subtelomeric regions, and (2) the mitochondrial genome, which lacks recombination and is maternally inherited. Together, these two genetic systems should be ideally suited to the study of similarities and dissimilarities between the population histories of males and females.

In order to test this empirically, we have studied Arab tribal groups in the Sinai Peninsula. According to the 1986 census, the population of Sinai is 220,000, of which ~70% belong to tribal groups in which Bedouin traditions play an important role. In particular, male polygamy and cousin marriages are frequent, and marriages generally take place within the tribe. When men occasionally marry women from outside the tribes, their children are incorporated into the man's tribe, whereas when a woman marries outside her tribe, the children become members of her husband's tribe (Specialised National Councils, Presidency of the Republic, Arab Republic of Egypt 1979; Abu-Zayed 1991). Thus, if this marriage system has been practiced for a long time, the effective population size of the mitochondrial and autosomal gene pool is expected to be large, since gene flow with outside populations, particularly from the Nile Delta and Valley, occurs through females. In contrast, the Y-chromosomal gene pool is expected to be

Table 1

Y-Chromosomal YAP/DXYS156Y/DYS19 Haplotype in Egyptian Populations in the Nile Valley and Sinai

	No. (%) with Haplotype														
	−/165/186	−/165/190	−/165/194	−/165/198	−/160/186	−/160/190	−/160/194	−/160/198	+/160/178	+/160/182	+/160/186	+/160/190	+/160/194	+/160/198	+/165/186
Sinai		65 (97.0)													2 (3.0)
Nile Valley	3 (2.0)	52 (34.0)	17 (11.1)	8 (5.2)	1 (0.7)	3 (2.0)	4 (2.6)	2 (1.3)	1 (0.7)	1 (0.7)	22 (14.4)	23 (15.0)	6 (3.9)	8 (5.2)	2 (1.3)
Mansoura		10 (45.5)	4 (18.2)					1 (4.6)			1 (4.6)	3 (13.4)	1 (4.6)	1 (4.6)	1 (4.6)
Asyut		5 (29.4)	5 (29.4)	1 (5.9)					1 (5.9)	1 (5.9)	1 (5.9)	2 (11.8)	1 (5.9)		
Sohag	3 (5.8)	15 (28.9)	2 (3.9)	7 (13.5)	1 (1.9)	2 (3.9)	1 (1.9)	1 (1.9)			9 (17.3)	8 (15.4)	2 (3.9)	1 (1.9)	

restricted to the tribal group—and, furthermore, to be restricted in effective size—through male polygamy.

Sixty-seven males from the El-Bayadia and El-Sawarka tribes in northern Sinai were studied with respect to three polymorphic loci on the nonrecombining portion of the Y chromosome: YAP (Hammer 1994), DXYS156Y (Chen et al. 1994), and DYS19 (Roewer et al. 1992). Table 1 shows that 65 men (97%) carry one and the same Alu/DXYS156Y/DYS19 haplotype (−/165/190). In contrast, among 153 men from the Nile Delta and Valley, 15 haplotypes are found. The haplotype that dominates in Sinai is also the most common there (34%), but others are also frequent (14% and 15%), such that the genetic diversity (Nei 1987) along the Nile is .83 whereas that of Sinai is .059. When local populations in the Nile Delta and Valley are studied, genetic diversity remains comparable to that of the pooled Egyptian sample (table 1). For example, the genetic diversity in Sohag, Asyut, and Mansoura is .85, .85, and .77, respectively. Thus, Y-chromosomal diversity in Sinai is ~14 times lower than that in the Nile Valley.

It is noteworthy that the same Y-chromosomal haplotype predominates in both tribal groups studied. This may be due to the fact that this haplotype is the most common also in the Nile Valley and thus most likely to have become frequent through drift in these small groups. Studies of further loci, as well as of other tribes, will show to what extent the Y-chromosomal gene pools of tribal groups differ.

In order to gauge mitochondrial diversity, a 360-bp-long hypervariable segment of the mtDNA control region was sequenced from 15 individuals of the El-Bayadia tribe and from 14 individuals of the El-Sawarka tribe. Twenty-four mitochondrial sequences were found (12 in each tribe). Among 46 individuals from Mansoura and 23 from Asyut, 42 and 22 sequences occurred, respectively. Thus, the mitochondrial diversity is as high in Sinai as in other Egyptian populations (~.9). When slowly evolving nucleotide positions (Hasagawa et al. 1993), which may reveal population bottlenecks in the past (A. Sajantila and S. Pääbo, unpublished data), were analyzed, the diversity of the Sinai population was still as high as that of other Egyptians.

In conclusion, genetic diversity of the Y-chromosomal gene pool is extremely low in Sinai whereas it is high in other areas of Egypt. By contrast, no reduction in diversity can be seen in the mitochondrial gene pool of Sinai. For two larger populations, Native Americans (Pena et al. 1995) and Finns (A. Sajantila and S. Pääbo, personal communication), reductions in Y-chromosomal diversity have also been described. However, in these cases, some reduction in mitochondrial diversity can also be seen (Pena et al. 1995; A. Sajantila and S. Pääbo, personal communication), which reflects past bottlenecks, which affected females and males, probably during colonization events. In the case of Sinai tribal groups, the social practices of male polygamy and patrilocal exogamy are probably solely responsible for the different amounts of genetic diversity in the male and female gene pool. Thus, the results show that traditional patterns of marriage must have been upheld over substantial time. The study of mitochondrial and Y-chromosomal genetic diversity, in conjunction with demographic modeling, will probably prove to be an excellent tool for the study of the age and impact of such marriage patterns.

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Nonsyndromic Cleft Lip With or Without Cleft Palate: New BCL3 Information

To the Editor:

We did not previously provide LOD scores for linkage assuming heterogeneity, as suggested by Ott (1991) for the linkage analysis of cleft lip with or without cleft palate (CL/P) and BCL3, ApoC2, and D19S178 in the paper by Stein et al. (1995). The results from analysis using the HOMOG program, allowing for heterogeneity under the reduced penetrance model, gave a maximum LOD score of 1.85 for ApoC2, 0.41 for BCL3, 0.03 for D19S178, and 1.72 for multipoint analysis in the interval. For the affecteds-only model, the values are 1.96 for ApoC2, 0.41 for BCL3, 0.01 for D19S178, and 1.44 for the multipoint analysis.

We also reanalyzed the linkage results from our study, following the suggestion of Murray (1995) that model-free linkage methods should be applied in the study of CL/P. We used both the multilocus (Weeks and Lange 1992) and single-locus versions (Weeks and Lange 1988) of the APM package to test for linkage and performed simulation studies using 2,000 replicates, to assess the significance of the test results. Results from an unweighted analysis gave evidence for linkage by using the multilocus approach ($P = .046$). When each locus was considered separately, D19S178 and BCL3 provided nonsignificant evidence for linkage ($P = .443$ and $P = .063$, respectively), while for ApoC2 significant evidence for linkage was found ($P = .025$). When the weight function, 1/(square root of the allele frequencies), was used, the multilocus significance level was $P = .007$. When each locus was considered separately, BCL3 provided nonsignificant evidence for linkage ($P = .157$), while D19S178 and ApoC2 provided significant findings ($P = .012$, and $P = .044$, respectively). The power to detect linkage using APM is reduced for BCL3 relative to the other markers, because of the limited number of alleles at this locus (Goldin and Weeks 1994).

Thirty sporadic CL/P cases and their parents were ascertained at the Children's Hospital of Pennsylvania. The ethnic distribution was 27 Caucasian, 1 Asian, and 2 African-American children. Analyses yielded evidence of a significant association between BCL3 and CL/P ($\chi^2_5 = 10.799$; $P = .030$). Allele 3 was preferentially transmitted (17 alleles transmitted vs. 6 nontransmitted, $P = .03$). For D19S178, the overall test for association yielded a significant result ($\chi^2_5 = 19.447$; $P = .017$). Allele 2 was more likely to be transmitted to affected children (14 alleles transmitted vs. 2 nontransmitted; $P = .004$).

In summary, these results support linkage and association between chromosome 19 markers in the vicinity of BCL3, using a variety of parametric (as previously reported) and nonparametric techniques, despite an error in our previous analysis using the transmission disequilibrium test. (Amos et al. 1996, in this issue).

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